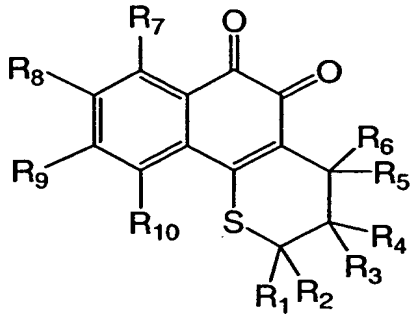
CLAIMS

We claim:

1. A compound of formula I:



I

or pharmaceutically acceptable salts thereof, or a regioisomeric mixture thereof, wherein

R1-R6 are each, independently, selected from the group consisting of H, OH, substituted and unsubstituted C_1-C_6 alkyl, substituted and unsubstituted C_1-C_6 alkenyl, substituted and unsubstituted C_1-C_6 alkoxy, substituted and unsubstituted C_1-C_6 alkoxycarbonyl, substituted and unsubstituted C_1-C_6 acyl, -$(CH_2)_n$-amino, -$(CH_2)_n$-aryl, -$(CH_2)_n$-heterocycle, and -$(CH_2)_n$-phenyl; or one of R1 or R2 and one of R3 or R4; or one of R3 or R4 and one of R5 or R6 form a fused ring, wherein the ring has 4-8 ring members;

R7-R10 are each, independently, hydrogen, hydroxyl, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, nitro, cyano or amide; and

n is an integer from 0 to 10.

2. The compound of claim 1, wherein R1 and R2 are alkyl, R3-R6 are, independently, H, OH, halogen, alkyl, alkoxy, substituted or unsubstituted acyl, substituted alkenyl or substituted alkyl carbonyl, and R7-R10 are hydrogen.

3. The compound of claim 1, wherein R1 and R2 are each methyl and R3-R10 are each hydrogen.

4. The compound of claim 1, wherein R1-R4 are each hydrogen, R5 and R6 are each methyl and R7-R10 are each hydrogen.

5. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 in combination with a pharmaceutically acceptable carrier.

6. A method of treating or preventing cell proliferative disorders comprising administering to a mammal in need thereof a therapeutically effective amount of the pharmaceutical composition of claim 5.

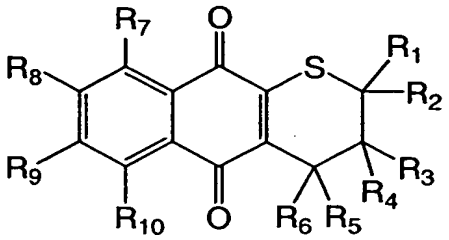
7. The method of claim 6, wherein administration induces sustained elevation of E2F levels in abnormally proliferating cells without affecting E2F levels in normal cells.

8. A method of treating cancer or precancerous conditions or preventing cancer comprising administering to a mammal in need thereof a therapeutically effective amount of a pharmaceutical composition of claim 5.

9. The method of claim 8, wherein administration induces sustained elevation of E2F levels in cancer cells without affecting E2F levels in normal cells.

10. A method of treating or preventing psoriasis comprising administering to a mammal in need thereof a therapeutically effective amount of a pharmaceutical composition of claim 5.

11. A compound of formula II:



II

or pharmaceutically acceptable salts thereof, or a regioisomeric mixture thereof, wherein

R1-R6 are each, independently, selected from the group consisting of H, OH, substituted and unsubstituted C_1-C_6 alkyl, substituted and unsubstituted C_1-C_6 alkenyl, substituted and unsubstituted C_1-C_6 alkoxy, substituted and unsubstituted C_1-C_6 alkoxycarbonyl, substituted and unsubstituted C_1-C_6 acyl, -$(CH_2)_n$-amino, -$(CH_2)_n$-aryl, -$(CH_2)_n$-heterocycle, and -$(CH_2)_n$-phenyl;

R7-R10 are each, independently, hydrogen, hydroxyl, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, nitro, cyano or amide; and

n is an integer from 0 to 10,

wherein when R1 and R2 are both methyl, R3 and R4 are both H, and one of R5 and R6 is OH and the other H, R7 is not methyl or methoxy and R10 is not methyl.

12. The compound of claim 11, wherein R1 and R2 are alkyl, R3-R6 are independently H, OH, halogen, alkyl, alkoxy, substituted and unsubstituted acyl, substituted alkenyl or substituted alkyl carbonyl, and R7-R10 are hydrogen.

13. The compound of claim 11, wherein R1 and R2 are each methyl and R3-R10 are each hydrogen.

14. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 11 in combination with a pharmaceutically acceptable carrier.

15. A method of treating or preventing cell proliferative disorders comprising administering to a mammal in need thereof a therapeutically effective amount of the pharmaceutical composition of claim 14.

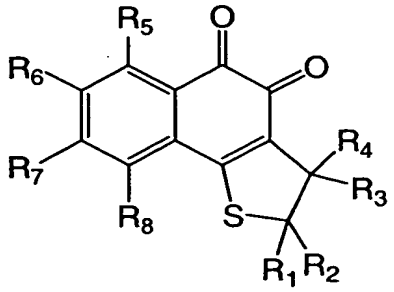
16. The method of claim 15, wherein administration induces sustained elevation of E2F levels in abnormally proliferating cells without affecting E2F levels in normal cells.

17. A method of treating cancer or precancerous conditions or preventing cancer comprising administering to a mammal in need thereof a therapeutically effective amount of a pharmaceutical composition of claim 14.

18. The method of claim 17, wherein administration induces sustained elevation of E2F levels in cancer cells without affecting E2F levels in normal cells.

19. A method of treating or preventing psoriasis comprising administering to a mammal in need thereof a therapeutically effective amount of a pharmaceutical composition of claim 14.

20. A compound of formula III:



III

or pharmaceutically acceptable salts thereof, or a regioisomeric mixture thereof, wherein

R1-R4 are each, independently, selected from the group consisting of H, OH, substituted and unsubstituted C_1-C_6 alkyl, substituted and unsubstituted C_1-C_6 alkenyl, substituted and unsubstituted C_1-C_6 alkoxy, substituted and unsubstituted C_1-C_6 alkoxycarbonyl, substituted and unsubstituted C_1-C_6 acyl, -$(CH_2)_n$-amino, -$(CH_2)_n$-aryl, -$(CH_2)_n$-heterocycle, and -$(CH_2)_n$-phenyl;

R5-R8 are each, independently, hydrogen, hydroxyl, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, nitro, cyano or amide; and

n is an integer from 0 to 10.

21. The compound of claim 20, wherein one of R1 and R2 is H and the other is alkyl, R3 and R4 are independently H, OH, halogen, alkyl, alkoxy, substituted or unsubstituted alkenyl or substituted or unsubstituted alkyl carbonyl, and R5-R8 are each hydrogen.

22. The compound of claim 20, wherein one of R1 and R2 is H and the other is alkyl, R3 and R4 are each methyl, and R5-R8 are each hydrogen.

23. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 20 in combination with a pharmaceutically acceptable carrier.

24. A method of treating or preventing cell proliferative disorders comprising administering to a mammal in need thereof a therapeutically effective amount of the pharmaceutical composition of claim 23.

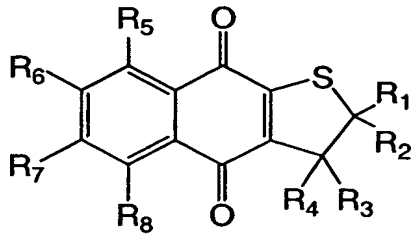
25. The method of claim 24, wherein administration induces sustained elevation of E2F levels in abnormally proliferating cells without affecting E2F levels in normal cells.

26. A method of treating cancer or precancerous conditions or preventing cancer comprising administering to a mammal in need thereof a therapeutically effective amount of a pharmaceutical composition of claim 23.

27. The method of claim 26, wherein administration induces sustained elevation of E2F levels in cancer cells without affecting E2F levels in normal cells.

28. A method of treating or preventing psoriasis comprising administering to a mammal in need thereof a therapeutically effective amount of a pharmaceutical composition of claim 23.

29. A compound of Formula IV:



IV

or pharmaceutically acceptable salts thereof, or a regioisomeric mixture thereof, wherein

R1-R4 are each, independently, selected from the group consisting of H, OH, substituted and unsubstituted C_1-C_6 alkyl, substituted and unsubstituted C_1-C_6 alkenyl, substituted and unsubstituted C_1-C_6 alkoxy, substituted and unsubstituted C_1-C_6 alkoxycarbonyl, substituted and unsubstituted C_1-C_6 acyl, -$(CH_2)_n$-amino, -$(CH_2)_n$-aryl, -$(CH_2)_n$-heterocycle, and -$(CH_2)_n$-phenyl;

R5-R8 are each, independently, hydrogen, hydroxyl, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, nitro, cyano or amide; and

n is an integer from 0 to 10,

wherein:

when R1 and R2 are both methyl, one of R3 and R4 is not methyl and the other H, and each of R5, R6, R7 and R8 is not H;

when R1 and R2 are both methyl, at least one of R3, R4, R5, R6, R7 and R8 is not H;

when R1 and R2 are both phenyl, at least one of R3, R4, R5, R6, R7 and R8 is not H;

when one of R1 and R2 is phenyl and the other is H, at least one of R3, R4, R5, R6, R7 and R8 is not H;

when one of R1 and R2 is phenyl and the other is methyl, at least one of R3, R4, R5, R6, R7 and R8 is not H;

when one of R1 and R2 is methyl and the other is H and R5, R6, R7 and R8 are H, at least one of R3 and R4 is not OH and the other H;

when one of R3 and R4 are carboethoxy the other is H; and

R1, R2, R3, R4, R5, R6, R7 and R8 are not each H.

30. The compound of claim 29 wherein, both R1 and R2 are substituted or unsubstituted alkyl, R3 and R4 are independently H, OH, halogen, alkyl, alkoxy, substituted or unsubstituted alkenyl or substituted or unsubstituted alkyl carbonyl, and R5-R8 are each hydrogen.

31. The compound of claim 29 wherein, one of R1 and R2 is H and the other is methyl, R3 and R4 are each methyl and R5-R8 are each hydrogen.

32. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 29 in combination with a pharmaceutically acceptable carrier.

33. A method of treating or preventing cell proliferative disorders comprising administering to a mammal in need thereof a therapeutically effective amount of the pharmaceutical composition of claim 32.

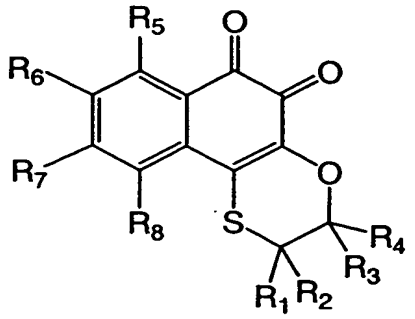
34. The method of claim 33, wherein administration induces sustained elevation of E2F levels in abnormally proliferating cells without affecting E2F levels in normal cells.

35. A method of treating cancer or precancerous conditions or preventing cancer comprising administering to a mammal in need thereof a therapeutically effective amount of a pharmaceutical composition of claim 32.

36. The method of claim 35, wherein administration induces sustained elevation of E2F levels in cancer cells without affecting E2F levels in normal cells.

37. A method of treating or preventing psoriasis comprising administering to a mammal in need thereof a therapeutically effective amount of a pharmaceutical composition of claim 32.

38. A compound of formula V:



V

or pharmaceutically acceptable salts thereof, or a regioisomeric mixture thereof, wherein

R1-R4 are each, independently, selected from the group consisting of H, substituted and unsubstituted C_1-C_6 alkyl, substituted and unsubstituted C_1-C_6 alkenyl, substituted and unsubstituted C_1-C_6 alkoxy, substituted and unsubstituted C_1-C_6 alkoxycarbonyl, substituted and unsubstituted C_1-C_6 acyl, -$(CH_2)_n$-amino, -$(CH_2)_n$-aryl, -$(CH_2)_n$-heterocycle, and -$(CH_2)_n$-phenyl; or one of R1 or R2 and one of R3 or R4 form a fused ring, wherein the ring has 4-8 ring members;

R5-R8 are each, independently, hydrogen, hydroxyl, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, nitro, cyano or amide; and

n is an integer from 1 to 10,

wherein R1, R2, R3, R4, R5, R6, R7 and R8 are not each H.

39. The compound of claim 40, wherein R1 and R2 are alkyl, R3-R4 are, independently, H, OH, halogen, alkyl, alkoxy, substituted or unsubstituted acyl, substituted alkenyl or substituted alkyl carbonyl, and R7-R10 are each hydrogen.

40. The compound of claim 40, wherein R1 and R2 are each hydrogen, one of R3 and R4 is methyl and the other is hydrogen and R5-R8 are each hydrogen.

41. The compound of claim 40, wherein one of R1 and R2 is methyl and the other is hydrogen, one of R3 and R4 is methyl and the other is hydrogen and R5-R8 are each hydrogen.

42. The compound of claim 40, wherein one of R1 and R2 is methyl and the other is hydrogen, one of R3 and R4 is hydroxymethyl and the other is hydrogen and R5-R8 are each hydrogen.

43. The compound of claim 40, wherein one of R1 and R2 is methyl and the other is hydrogen, R3 and R4 are each methyl and R5-R8 are each hydrogen.

44. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 40 in combination with a pharmaceutically acceptable carrier.

45. A method of treating or preventing cell proliferative disorders comprising administering to a mammal in need thereof a therapeutically effective amount of the pharmaceutical composition of claim 44.

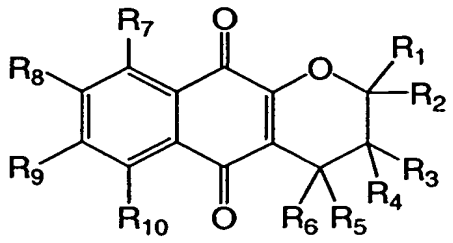
46. The method of claim 45, wherein administration induces sustained elevation of E2F levels in abnormally proliferating cells without affecting E2F levels in normal cells.

47. A method of treating cancer or precancerous conditions or preventing cancer comprising administering to a mammal in need thereof a therapeutically effective amount of a pharmaceutical composition of claim 44.

48. The method of claim 47, wherein administration induces sustained elevation of E2F levels in cancer cells without affecting E2F levels in normal cells.

49. A method of treating or preventing psoriasis comprising administering to a mammal in need thereof a therapeutically effective amount of a pharmaceutical composition of claim 44.

50. A method for the synthesis of a compound of Formula I comprising:
reacting a compound having the Formula A:



A

wherein R1-R6 are each, independently, selected from the group consisting of H, OH, substituted and unsubstituted C_1-C_6 alkyl, substituted and unsubstituted C_1-C_6 alkenyl, substituted and unsubstituted C_1-C_6 alkoxy, substituted and unsubstituted C_1-C_6 alkoxycarbonyl, substituted and unsubstituted C_1-C_6 acyl, -$(CH_2)_n$-amino, -$(CH_2)_n$-aryl, -$(CH_2)_n$-heterocycle, and -$(CH_2)_n$-phenyl;

R7-R10 are each, independently, hydrogen, hydroxyl, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, nitro, cyano or amide; and

n is an integer from 0 to 10,

with sodium hydrosulfide to exchange oxygen for sulfur and forming the di-thione of the compound of Formula A;

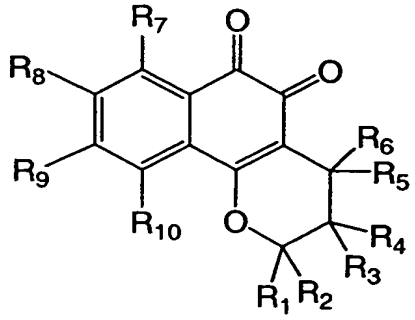
and,

reacting said di-thione of the compound of Formula A with a strong acid to form a compound of Formula I.

51. The method of claim 50, wherein said strong acid is concentrated sulfuric acid.

52. A method for the synthesis of a compound of Formula II comprising:

reacting a compound having the Formula B:



B

wherein R1-R6 are each, independently, selected from the group consisting of H, OH, substituted and unsubstituted C_1-C_6 alkyl, substituted and unsubstituted C_1-C_6 alkenyl,

substituted and unsubstituted C_1-C_6 alkoxy, substituted and unsubstituted C_1-C_6 alkoxycarbonyl, substituted and unsubstituted C_1-C_6 acyl, -$(CH_2)_n$-amino, -$(CH_2)_n$-aryl, -$(CH_2)_n$-heterocycle, and -$(CH_2)_n$-phenyl;

R7-R10 are each, independently, hydrogen, hydroxyl, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, nitro, cyano or amide; and

n is an integer from 0 to 10,

wherein when R1 and R2 are both methyl, R3 and R4 are both H, and one of R5 and R6 is OH and the other H, R7 is not methyl or methoxy and R10 is not methyl,

with sodium disulfide to exchange oxygen for sulfur and forming the di-thione of the compound of Formula B;

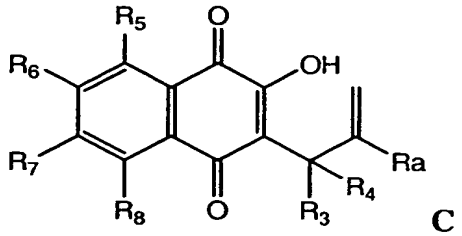
and,

reacting said di-thione of the compound of Formula B with a strong acid to form a compound of Formula II.

53. The method of claim 52, wherein said strong acid is concentrated sulfuric acid.

54. A method for synthesizing a compound of formula III, comprising

reacting a compound having the Formula C:



C

wherein Ra is selected from R1 and R2;

R1-R4 are each, independently, selected from the group consisting of H, OH, substituted and unsubstituted C_1-C_6 alkyl, substituted and unsubstituted C_1-C_6 alkenyl, substituted and unsubstituted C_1-C_6 alkoxy, substituted and unsubstituted C_1-C_6 alkoxycarbonyl, substituted and unsubstituted C_1-C_6 acyl, -$(CH_2)_n$-amino, -$(CH_2)_n$-aryl, -$(CH_2)_n$-heterocycle, and -$(CH_2)_n$-phenyl;

R5-R8 are each, independently, hydrogen, hydroxyl, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, nitro, cyano or amide; n is an integer from 0 to 10

with sodium hydrosulfide to form the di-thione of the compound of Formula C,

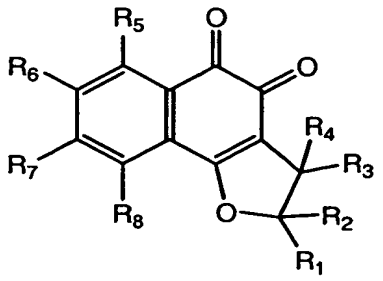
and,

treating said di-thione of compound of Formula C with a strong acid to form a compound of Formula III.

55. The method of claim 54, wherein said strong acid is concentrated sulfuric acid.

56. A method for synthesizing a compound of formula IV,

reacting a compound having the Formula D:



D

R1-R4 are each, independently, selected from the group consisting of H, OH, substituted and unsubstituted C_1-C_6 alkyl, substituted and unsubstituted C_1-C_6 alkenyl, substituted and unsubstituted C_1-C_6 alkoxy, substituted and unsubstituted C_1-C_6 alkoxycarbonyl, substituted and unsubstituted C_1-C_6 acyl, -$(CH_2)_n$-amino, -$(CH_2)_n$-aryl, -$(CH_2)_n$-heterocycle, and -$(CH_2)_n$-phenyl;

R5-R8 are each, independently, hydrogen, hydroxyl, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, nitro, cyano or amide; and

n is an integer from 0 to 10,

wherein:

when R1 and R2 are both methyl, one of R3 and R4 is not methyl and the other H, and each of R5, R6, R7 and R8 is not H;

when R1 and R2 are both methyl, at least one of R3, R4, R5, R6, R7 and R8 is not H;

when R1 and R2 are both phenyl, at least one of R3, R4, R5, R6, R7 and R8 is not H;

when one of R1 and R2 is phenyl and the other is H, at least one of R3, R4, R5, R6, R7 and R8 is not H;

when one of R1 and R2 is phenyl and the other is methyl, at least one of R3, R4, R5, R6, R7 and R8 is not H;

when one of R1 and R2 is methyl and the other is H and R5, R6, R7 and R8 are H, at least one of R3 and R4 is not OH and the other H;

when one of R3 and R4 are carboethoxy the other is H; and

R1, R2, R3, R4, R5, R6, R7 and R8 are not each H,

with sodium hydrosulfide to form the di-thione of the compound of Formula D,

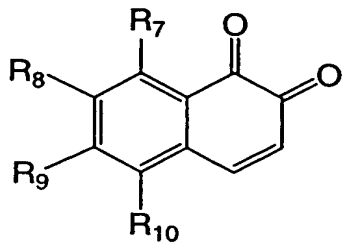
and,

treating said di-thione of the compound of Formula D with a strong acid to form a compound of Formula IV.

57. The method of claim 56, wherein said strong acid is concentrated sulfuric acid.

58. A method for the synthesis of a compound of Formula I comprising:

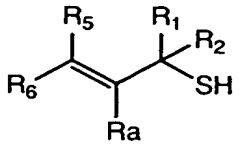
reacting a compound having the Formula E:



E

wherein R7-R10 are each, independently, hydrogen, hydroxyl, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, nitro, cyano or amide,

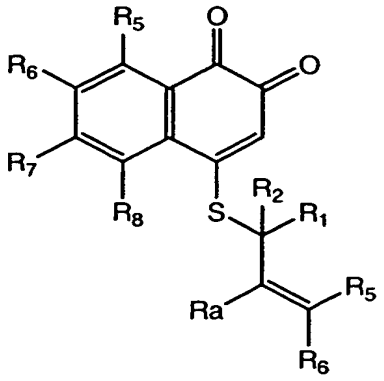
with a branched allylthiol having the formula:



wherein Ra is selected from R3 and R4;

R1-R6 are each, independently, selected from the group consisting of H, OH, substituted and unsubstituted C_1-C_6 alkyl, substituted and unsubstituted C_1-C_6 alkenyl, substituted and unsubstituted C_1-C_6 alkoxy, substituted and unsubstituted C_1-C_6 alkoxycarbonyl, substituted and unsubstituted C_1-C_6 acyl, -$(CH_2)_n$-amino, -$(CH_2)_n$-aryl, -$(CH_2)_n$-heterocycle, and -$(CH_2)_n$-phenyl; and, and n is an integer from 0 to 10,

in the presence of a weak base to form the sulfide intermediate having the formula:



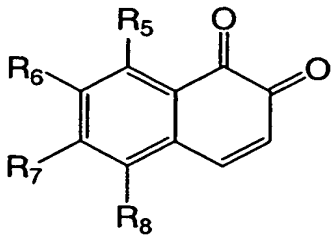
and,

treating said sulfide intermediate with a strong acid to form the a compound of Formula I.

59. The method of claim 58, wherein the weak base is triethylamine.

60. The method of claim 58, wherein said strong acid is concentrated sulfuric acid.

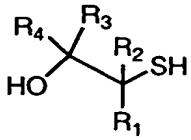
61. A method for the synthesis of a compound of Formula III comprising:
reacting a compound having the Formula F:



F

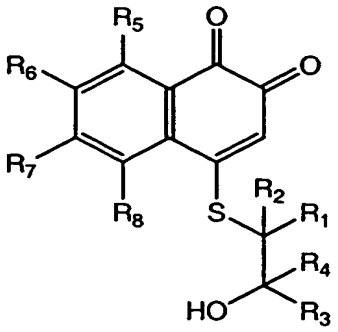
wherein R5-R8 are each, independently, hydrogen, hydroxyl, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, nitro, cyano or amide,

with 2-hydroxyalkylthiol having the formula:



wherein R1-R4 are each, independently, selected from the group consisting of H, substituted and unsubstituted C_1-C_6 alkyl, substituted and unsubstituted C_1-C_6 alkenyl, substituted and unsubstituted C_1-C_6 alkoxycarbonyl, -$(CH_2)_n$-amino, -$(CH_2)_n$-aryl, -$(CH_2)_n$-heterocycle, -$(CH_2)_n$-phenyl, aryl, heterocycle, and phenyl; and n is an integer from 1 to 10

in the presence of a weak base to form a sulfide intermediate having the formula:



and,

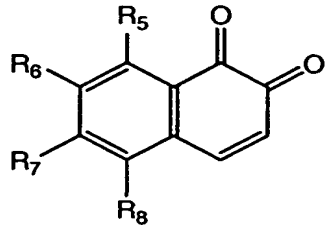
treating said sulfide intermediate with a strong acid to form the a compound of Formula III.

62. The method of claim 61, wherein the weak base is triethylamine.

63. The method of claim 61, wherein said strong acid is concentrated sulfuric acid.

64. A method for synthesizing a compound of Formula V, comprising:

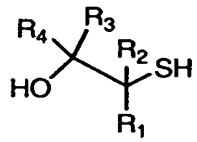
reacting a compound having the Formula G:



G

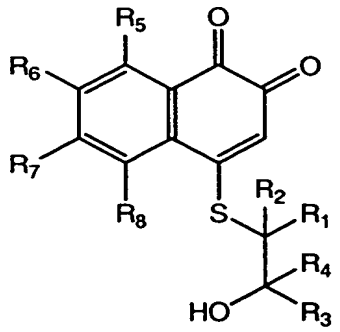
wherein R5-R8 are each, independently, hydrogen, hydroxyl, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, nitro, cyano or amide,

with a 2-hydroxyalcohol having the formula:



wherein R1-R4 are each, independently, selected from the group consisting of H, substituted and unsubstituted C_1-C_6 alkyl, substituted and unsubstituted C_1-C_6 alkenyl, substituted and unsubstituted C_1-C_6 alkoxy, substituted and unsubstituted C_1-C_6 alkoxycarbonyl, substituted and unsubstituted C_1-C_6 acyl, -$(CH_2)_n$-amino, -$(CH_2)_n$-aryl, -$(CH_2)_n$-heterocycle, and -$(CH_2)_n$-phenyl; n is an integer from 1 to 10,

to form a sulfide having the formula:



and,

treating said sulfide with strong acid and exposing the reaction to air to form a compound of Formula V.

65. The method of claim 64, wherein said strong acid is concentrated sulfuric acid or trifluoroacetic acid.